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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,514	12/21/2000	Paul V. Phibbs	5218.87	1007

20792 7590 07/18/2002

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	7

DATE MAILED: 07/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,514	PHIBBS ET AL.	
	Examiner	Art Unit	
	Terra Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) 10-15 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-15 are pending in the instant application.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "said bacteria" or "said compound".

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9, drawn to a method of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria, comprising administering to said bacteria a test compound in an effective antivirulence amount, classifiable in class 435, subclass 6, for example.

II. Claims 10-15, drawn to a method of treating *Pseudomonas* infection in a subject in need thereof, comprising administering to said subject an antisense oligonucleotide that inhibits

Pseudomonas Crc expression in an effective amount effective to treat said *Pseudomonas* infection, classifiable in class 514, subclass 44 and class 536 subclass 24.5, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I (claims 1-9) and II (claims10-15) are unrelated, each from the other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions are drawn to a *method of screening* (Group I) for compounds that inhibit the virulence of *Pseudomonas* bacteria and a *method of treating* (Group II) *Pseudomonas* infection in a subject in need thereof, comprising administering to said subject an antisense oligonucleotide in an amount effective to treat said *Pseudomonas* infection. In the instant case the different inventions are not disclosed as capable of use together and have different operations, functions and effects. The two methods have different and noninterchangable steps that lead to different ends (e.g. compound discovery vs. treatment of infection). Further, the method of Group I encompass the use of compounds not used in Group II, for example.

Because these inventions are distinct for the reasons given above and the sequence search required for each of Groups I and II are not required for the other Groups, restriction for examination purposes as indicated is proper.

During a telephone conversation with Attorney Kenneth Sibley on 6/26/02, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-9. Affirmation of this election must be made by applicant in replying to this Office action. Claims 10-15 are

withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Claims 1-9 are examined as they read on the elected subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bright et al. (a) (Abstract, 96th ASM General Meeting, pp. 220 (1996), Bright et al. (b) (Abstract, 1995 Cystic Fibrosis Conference pp. 225), and further in view of Mahan et al. [US Patent Application No. 09/927885], MacGregor et al. (Journal of Bacteriology, 1996 pp. 5627-5635), O'Toole et al. (Journal of Bacteriology, 2000 pp. 425-431), and Arrow et al. [WO Patent No. 98/03533].

Claims 1-9 are drawn to a method of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria and detecting the presence or absence of inhibition of the catabolite repression control (Crc) protein.

Bright et al. (a) have taught crc mutants of *Pseudomonas* aeruginosa have alterations in the production of diverse virulence factors. Bright et al. (a) have further taught the study of crc mutants, PAO8020, DB101 and AP331 show a correlation between crc and virulence in a mouse model of pneumonia.

Bright et al. (b) have taught the involvement of the crc locus in the regulation of the expression of *Pseudomonas* aeruginosa virulence factors. Bright et al. (b) have further taught a crc deletion mutant, PAO8020 was tested for expression of virulence factors.

Mahan et al. have taught a method of screening for agents that have anti-bacterial activity (see page 6, [0054]). Mahan et al. have further taught a method of reducing bacterial virulence comprising: contacting bacteria with an agent that alters the bacteria's native level of DNA methyltransferase activity (see Claim No: 1).

Bright et al. (a) and (b) and Mahan et al. have not taught detecting the presence or absence of inhibition of the catabolite repression control (Crc) protein in an inhibitor of virulence assay.

MacGregor et al. and O'Toole et al. have taught methods of detecting the presence or absence of inhibition of the catabolite repression control (Crc) protein were known at the time of invention.

MacGregor et al. have taught the identification of crc protein in PAO1 and various crc mutant strains (see Figure 9). MacGregor et al. have further taught knockout crc mutants lack cross-reacting proteins and contain nonfunctional proteins of crc.

O'Toole et al. have taught fluoroacetamide (FAA) sensitivity acts as an indirect assay of crc function (see, page 428, last paragraph). O'Toole et al. have further taught crc mutants are sensitive to growth on succinate-containing medium supplemented with FAA (Figure 4).

Arrow et al. have taught the use of oligonucleotides to inhibit the growth of intact clinically relevant bacteria (see page 16, lines 14-17). Arrow et al. have further taught, "the oligonucleotides generally inhibit bacterial growth by acting as antisense... or by acting aptamerically to alter the function of specific bacterial proteins or polypeptides" (see page 16, lines 16-21).

In view of Bright et al. (a), Bright et al. (b), Mahan et al., MacGregor et al., O'Toole et al. and Arrow et al. it would have been obvious to devise a method of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria and detecting the presence or absence of inhibition of the catabolite repression control (Crc) protein. One of ordinary skill in the art would have been motivated to devise a method of screening for compounds that inhibit the virulence of

Pseudomonas bacteria since the prior art has indicated the desirability of screening methods that reduce bacterial virulence (Mahan et al.). Since Bright et al. (a) and (b) have taught the involvement of the crc locus in the regulation of the expression of *Pseudomonas* aeruginosa virulence factors, one of ordinary skill in the art would have been motivated to include catabolite repression control (crc) proteins in an assay for virulence inhibitors. One of ordinary skill in the art would have chosen a method of detecting the presence or absence of inhibition of crc protein and had a reasonable expectation of success since the art has taught the identification of crc protein in various crc mutant strains and FAA sensitivity as an assay of crc function (MacGregor et al and O'Toole et al.). One of ordinary skill in the art would have been motivated to include oligonucleotides as inhibitors of bacterial virulence since Arrow et al. have taught the use of oligonucleotides to inhibit the growth of bacteria.

The invention as a whole would therefore have been obvious to one or ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SEAN McGARRY
PRIMARY EXAMINER